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10/815,107	03/31/2004	Mangala Gowri Ponnappalli	U 015131-4	6583
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EXAMINER				
MCCORMICK, MELENIE LEE				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

10/815,107

Applicant(s)

PONNAPALLI ET AL.

Examiner

MELENIE MCCORMICK

Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 9-12 and 14-20 is/are pending in the application.
- 4a) Of the above claim(s) 12 and 15-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 9-11, 14 and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's remarks with claim amendments submitted 06 November 2008 have been received and considered.

Claim 13 has been cancelled. Claims 6 and 8 were previously cancelled.

Claims 1-5, 7, 9-12 and 14-20 are pending.

Claims 12 and 15-19 stand withdrawn.

Claims 1-5, 7, 9-11, 14 and 20 are presented for examination on the merits.

Election/Restrictions

Applicants argue that the restriction of claims 12 and 15-19 should be withdrawn. Applicants argue that all of the claims are dependent upon claim 1 and therefore cannot be distinct from it or present a different invention. As stated in the previous Office Action, claims 12 and 15-19 (which were newly presented before the previous Office Action) are drawn to different methods which have different designs than the originally presented method. As previously stated, claim 12 appears to be directed to a method of screening fruits, which contains steps that are not used in the method of claim 1. In addition, claims 15-19 are directed to direct extraction with EDC/DCM and by using dry processes, which are not used in extraction method disclosed in claim 1. These methods are therefore distinct from the method of claim 1 because they require different steps than the method of claim 1 and do not appear to require the method of claim 1, even though they are dependent upon claim 1. Although Applicants agree that these

methods are related to the steps set out in claim 1, it is not apparent where these methods steps occur in the method of claim 1 and it appears they are directed to different methods from the method of claim 1.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 12 and 15-19 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

The restriction is therefore made final.

It is noted that Applicant has not directly responded to the rejection under 35 U.S.C. 112, second paragraph. It appears claim amendments have been made in an attempt to overcome the rejection.

Withdrawn Rejections

The previous objection to claims 4 and 5 has been withdrawn since the claims now end in a period, rather than a semicolon.

The previous objection to claim 1 has been withdrawn in light of the amendment changing 'in' to 'to' in step c.

The previous objection to claims 10-11 has been withdrawn in light of the

amendment which expresses the ratios with colons rather than periods.

The previous rejection to claim 14 under 35 U.S.C. 112, second paragraph has been withdrawn in light of Applicant's statement on page 1 of the most recent remarks that 'bulkiness' is understood in the art to mean mass.

The previous rejection of claim 7 under 112, second paragraph is withdrawn, as the term 'range' was deleted from the claims in the previous claim set.

The previous rejection of claim 20 under 35 U.S.C. 112, second paragraph has been withdrawn in light of the addition of the term 'from' before 'mature fruits', 'immature fruits', and 'ripe fruits' because it is now clear that the amounts isolated are isolated from those fruits. The claim is also now clear with respect to when the extraction in Soxhlet apparatus with ethylenedichloride occurs.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1- 5, 7, and 9-11, 14 and 19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saha et al. (1957) in view of Bastnet et al. (2001) and in view

of Bizhanova et al. (1977) for the reasons set forth in the previous Office Action, which are discussed below.

Saha et al. beneficially teach a method of isolating imperatorin which comprises the steps of extracting fruit pulp of *Angle marmelos* with alcohol under reduced pressure (which would concentrate the alcoholic extract), and then freeing the extracted pulp from alcohol under reduced pressure and soxhletting with benzene (the step of freeing the extract from alcohol and then extracting in another solvent would to 'partition' the extract from the alcohol to the benzene, which would necessarily reduce the volume of the alcohol extract). Saha et al. further teaches that the extract is then dried over anhydrous sodium sulfate and concentrated (thus the solvent would be removed). Saha further teaches that the extract is then crystallized in ethanol (see e.g. 229 –isolation of Alloimperatorin). Saha et al also teaches that the mother liquid left over after the crystallization is then chromatographed over a column of alumina and then eluted with benzene and crystallized with petroleum ether. It is further disclosed that this elution and crystallization is repeated and multiple fractions are collected. (see e.g. page 229- Isolation of Imperatorin).

Saha et al. do not explicitly teach that a halogenated solvent is used or that a silica gel column is used.

Bastnet et al. beneficially teach that imperatorin is found in the chloroform soluble fraction of a methanolic extract of a plant (see e.g. abstract).

Bizhanova et al. beneficially teach that imperatorin can be isolated after alcoholic extraction using a silica gel column (see .g. English Abstract).

It would have been obvious to one of ordinary skill in the art to optionally select another non-polar solvent besides the benzene used by Saha in the method of isolating imperatorin taught by Saha. A person of ordinary skill in the art at the time the claimed invention was made would have had a reasonable expectation of success in substituting chloroform for the benzene taught by Saha because Bastnet discloses that imperatorin is soluble in chloroform. Thus, a person of ordinary skill in the art would have a reasonable expectation of success in isolating imperatorin using chloroform. A person of ordinary skill in the art would have also had a reasonable expectation of success in using silica gel column chromatography instead of alumina since Bizhanova et al. also teach teaches that after an alcoholic extraction, imperatorin can be separated using silica gel. The particular mesh size would be routine experimentation since the compound being isolated (imperatorin) is known. Although the filtration step instantly claimed in steps e and f of claim 1 is not explicitly taught by Saha et al., the removal of the crystals from the 'mother liquid' would suggest to one of ordinary skill in the art that filtrations must have taken place. Although the particular type of fruit pulp (i.e. immature/mature or dry/fresh) is not explicitly taught, a person of ordinary skill in the art would have a reasonable expectation of success in using what is readily available, which would inevitably be one of the instantly claimed types of *Angle marmelos*. It is also considered routine experimentation to optimize the time which is spent on extraction and the particular pulp to solvent ratio depending upon the yield of imperatorin which is desired. Although the particular yield of imperatorin after the soxhletting step taught by Saha is not explicitly taught and the amount of time spent

soxhletting is not taught, a person of ordinary skill in the art would have a reasonable expectation of success in optionally adjusting the amount of time spent during any step in the extraction process in order to improve the yield of the desired product.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicants have summarized their invention. Applicants have also summarized the teaching of Saha et al., Basnet et al., and Bizhanova et al.

Applicants argue that the filtrate is subjected to vacuum liquid filtration chromatography on silica gel and imperatorin eluted in a solvent to obtain a phytosterol enriched fraction and pure imperatorin fraction (see page 8 of remarks). The claims, however, do not state that a separate fraction containing only imperatorin is obtained. For example, claim 1, steps g-h state: 'g) eluting imperatorin in a solvent to afford a phytosterols enriched fraction and pure imperatorin' and 'h) crystallizing the fractions containing imperatorin'. The claims as written, however, do not require that the 'pure imperatorin' is in a fraction separate from the phytosterols fraction.

Applicants also argue that use of the claimed invention gives yields of 3.1%, 0.89% and 1.71% for mature, immature and ripe fruits respectively and that the claimed invention teaches efficient use and economical extraction of imperatorin with high purity (85% and 90% -example 3) and better yield of product as compared to the prior art. Applicants argue that the immunologically important phytosterol mixture enriched fractions were useful by products and that the use of the halogenated solvent in the present invention avoids problems associated with the use of benzene. Any by products obtained by the claimed method would also be obtained by the method rendered obvious by the prior art because the same method steps as the method steps instantly claimed would be performed in view of the prior art. The use of a halogenated solvent is obvious in light of the teaching of Basnet et al. that imperatorin is found in the chloroform soluble fraction of a methanolic extract of a plant (see e.g. abstract). A person of ordinary skill in the art at the time the claimed invention was made would have had a reasonable expectation of success in substituting chloroform for the benzene taught by Saha because Basnet discloses that imperatorin is soluble in chloroform. Thus, a person of ordinary skill in the art would have a reasonable expectation of success in isolating imperatorin using chloroform. Applicants argue that Saha et al. use an expensive process and results in poor yield. Applicants have not disclosed why this process is expensive of results in pure yield. Saha et al disclosed a method very similar to the method claimed, with the exception that Saha et al. do not explicitly teach that a halogenated solvent is used or that a silica gel column is used. These teachings were provided by Basnet and Bozhanova. Applicants also argue that Basnet et al. teach

imperatorin in the presence of other compounds and that Bizhanova et al. teach imperatorin in the presence of other compounds. Basnet et al. was relied upon for the teaching that imperatorin is soluble in chloroform. Therefore, it would be an obvious choice of extraction solvent since it was known that the compound of interest is soluble in chloroform. Applicants argue that the claimed invention yields higher purity than the processes of the prior art and demonstrates advantages not taught by the prior art. The purity of the imperatorin which results from the method instantly claimed is not defined as 100% pure. The term 'pure' as claimed is given the broadest reasonable interpretation in light of the specification. The specification states that 85% pure or 90% pure imperatorin was obtained from mature fruits (see e.g. Example 3 pages 15-16) and that 82% pure imperatorin was obtained from immature fruits (see e.g. example 4, pages 16-17). Therefore, the term 'pure' is interpreted to mean purified, but not absolutely pure in the sense that no other components are present. Therefore, the imperatorin which would be obtained by the method rendered obvious from the instantly cited references would also be purified, even if other compounds are present in the fraction isolated.

The rejection is therefore deemed proper and is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **MELENIE MCCORMICK** whose telephone number is (571)272-8037. The examiner can normally be reached on M-F 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Patricia Leith/
Primary Examiner, Art Unit 1655